(f) a volatile solvent;

wherein upon application on a nail, the volatile solvent evaporates and a film coating forms on the surface of the nail, the film coating releasing the antifungal and keratolytic agents in therapeutic levels over a prolonged period of time and trapping water in contact with the nail; the humectant retaining the water in the film; and said keratolytic agent and said water facilitating penetration of the released antifungal agent beyond the nail surface.

97. (New) The sustained-release therapeutic nail varnish composition of claim 96 further comprising an excipient.

REMARKS

Reconsideration of the above identified application, in view of the above amendments and the following remarks, is respectfully requested.

Description and Support For the Present Amendment

Claim 1 is amended to recite that the pharmaceutically effective agent is selected from the group consisting of antifungal agents, keratolytic agents, and mixtures thereof, i.e., to incorporate the subject matter of canceled claim 2. Claims 1 and 47 have been amended to recite that the composition of the present invention contains greater than 3% of a humectant. Support for this amendment is found on page 23, line 5. Claims 3, 5, 7, 8, 9, 10, and 11 have been amended to depend from

claim 1 instead of canceled claim 2.

Claims 94-97 have been added. Support for the newly added claims is found on page 18, lines 4-7, page 18, lines 11-14, page 18, line 18 to page 19, line 1, and page 22, lines 10-14 of the present specification.

Claims 1-97 are pending.

Rejection Under 35 U.S.C.§ 112

Claims 1, 6, 47, and 93 are rejected under 35 U.S.C. § 112, second paragraph as indefinite. The Examiner asserts that the phrase "a prolonged effect therapeutic nail composition" is vague and indefinite.

Claims 1, 47, and 93 have been amended, as suggested by the Examiner, to recite "a sustained-release therapeutic nail varnish composition" instead of "a prolonged effect therapeutic nail varnish composition". Since the terms "sustained-release" and "prolonged effect" are used interchangably in the instant specification, this amendment is not narrowing. Claim 93 has also been amended to correct the antecedent basis for humectant and polymeric film forming agent and to clarify that the pharmaceutical effective agents are keratolytic and antifungal agents. Support for this amendment is found on page 9, lines 8-10. Claim 6 is amended to correct the antecedent basis for the "non-volatile components". This is not a narrowing amendment.

In light of the action taken, Applicants respectfully request withdrawal of

this rejection.

Rejection Under 35 U.S.C.§ 103

Claims 1-93 are rejected under 35 U.S.C.§ 103 as obvious over Bohn (U.S. Patent No. 5,264,206) in view of Friedman (U.S. Patent No. 5,160,737). The Examiner contends that Bohn teaches a nail lacquer composition for treating mycoses of the nails (col. 1, lines 6-54 and col. 2, lines 46-68), comprising antifungal agents consisting of econazole, miconazole and naftifine hydrochloride (see Abstract, col. 3, lines 15-68 and the TABLE at col. 6, EXAMPLE 1-6), volatile solvents (col. 4, lines 46-68, bridging col. 5, lines 1-8), additives which are excipients (col. 5, lines 9-16), lanolin derivatives, urea and allantoin which have humectant properties (col. 5, lines 9-20), water (col. 6, EXAMPLES 7-9), film forming agents which include copolymers of methyl vinyl ether, copolymers of acrylic acid and methacrylic acid (col. 2, lines 58-68, bridging col. 3, lines 1-11) and keratolytic agents (i.e. salicylic acid) col. 5, lines 17-20). The Examiner acknowledges that Bohn does not teach a sustained release therapeutic nail varnish composition, but relies on Friedman to disclose a liquid methacrylic acid polymer composition containing sustained-release of pharmacological active agents (see Abstract) which are known in the art for treating dermatological conditions "of the skin". The Examiner concludes that it would have been obvious to one of ordinary skill in the art at the time the invention was made to use a sustained release composition taught by Friedman which is known in the art for treating

conditions "of the skin", in a nail varnish composition taught by Bohn et al.

This rejection is traversed, and reconsideration is respectfully requested.

First, the Examiner's attention is directed to the fact that fungal infections of the nail are notoriously treatment resistant (see American College of Foot and Ankle Surgeons website information, page 2 attached as Exhibit A). In fact, various commercially available antifungal compositions effective on the skin contain disclaimers that they are ineffective for fungal infections of the nail (see package insert for Lamisil ®AT, attached as Exhibit B).

With respect to claim 1 (and dependent claims 2-46 and 94), the present invention is directed to a composition for treating nail fungus comprising the unique, specific and advantageous combination of (i) an humectant and (ii) water in combination with an antifungal agent and/or a keratolytic agent. While a humectant and water are common ingredients of a wide variety of formulations, in this particular instance they play an important role of increasing the penetration of the active antifungal agent through the nail layers and thus providing better pharmacological action. This formulation in particular features a film-forming agent and a humectant, preferably glycerol, for trapping and maintaining water in the film formed on the nail, and the water so trapped and maintained continues to hydrate the nail for delivery of the agent thereto (page 7, lines 9-12 of the present specification). As shown in Example 2 (page 31) of the instant specification, compositions of the present invention made without an humectant entrapped and maintained substantially less water in the

film than compositions containing the humectant.

With respect to claims 47 and 93 (and dependent claims 48-92), the invention is directed to a composition for treating nail fungus, comprising the unique, specific and advantageous combination of (i) an antifungal agent, (ii) a keratolytic agent, (iii) an humectant, and (iv) water. In this embodiment, the humectant interacts with the keratolytic agent and trapped water to enhance the efficacy of the composition by increasing the penetration of the active antifungal agent through the nail layers, and thus providing better pharmacological action (see page 6, lines 6-10 of the specification).

Bohn et al. provides a laundry list of a variety of classes of ingredients and therefore contains no teaching to select the particular types of ingredients claimed. The presently claimed composition contains a humectant as a necessary, not an optional ingredient. The substances relied on by the Examiner at Bohn col. 5, lines 9-20, which she asserts have humectant and keratolytic properties, are disclosed as *optional* ingredients. From the Bohn list of a dozen possible ingredients recited by the Examiner, hundreds of combinations of one or more ingredients are possible. In the absence of some teaching about the methods to be used in selecting an appropriate combination for a composition for treating fungal infections of the nail, not merely on the skin, there is no hint that the presently claimed combination would, upon application to a nail and evaporation of the volatile solvent, trap and maintain water that is in contact with the nail, and deliver an antifungal agent below the nail surface,

where it can be more effective.

The compositions of Friedman et al. are directed to sustained-release formulations for use in the oral cavity or on skin. Friedman et al. discuss "dermatological uses" from col. 20, line 66 to col. 21, line 63, but do not address the particular use of their formulations on nails or as a nail varnish, nor do they exemplify any nail treatment formulations. Since, as discussed above, fungal nails are different from fungal skin, the formulations used to treat fungal infections of the skin are not generally effective in treating fungal infections of the nail. As discussed at page 3, lines 7-11 of the instant specification, permeability and penetration of antifungal agents through the nails has been especially difficult with conventional products, which has prompted researchers to resort to antifungal formulations for systemic administration for the treatment of fungal infections of the nails. These have serious side effects. See, e.g., the side effects associated with Lamisil® tablets, a copy of the package insert, taken from the 2001 Physician Desk Reference is attached at Exhibit C. Since antifungal formulations used on skin are different than those used on nails, one skilled in the art would not be motivated to apply teachings about a composition for use in the skin, willy nilly to a nail varnish as suggested by the Examiner.

In any event, the compositions disclosed by Friedman et al appear to be intended for use in the oral cavity, and do not contain glycerol or antifungal agents. Friedman et al. disclose the possibility of using glycerol, among many other possibilities, as a release adjusting agent (col. 12, lines 34-42). Friedman et al. also

describe glycerol as a demulcent/ humectant in concentrations of about 1% by weight

(col 16, lines18-21). Friedman et al. do not provide any motivation or suggestion for using their sustained-release system in a nail varnish which would be more effective in treating nail fungus by trapping and maintaining water in contact with the nail and thus increasing the penetration and efficacy of an antifungal agent.

The surprising and unexpected property of trapping and maintaining water in contact with the nail and harnessing the water together with keratolysis to enhance penetration of the antifungal agent is afforded only by the unique combination of ingredients of the present invention. The teachings of Bohn et al. and Friedman et al. fall short of suggesting such a combination.

Therefore, in view of the above amendments and remarks, it is respectfully requested that the application be reconsidered and that all pending claims be allowed and the case passed to issue.

If there are any other issues remaining which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the

Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

Respectfully submitted,

Mary Elizabeth Brown
Reg. No. 46,579
Attorney for Applicants

DARBY & DARBY, P.C.
805 Third Avenue
New York, N.Y. 10022
Phone (212) 527-7700